REMARKS

Applicant respectfully requests reconsideration of the pending claims in view of the foregoing amendments and the remarks that follow.

Status of the claims

Claims 1-102 were pending in the subject application. Claims 1-88 were previously withdrawn. Claims 89, 91 and 93 are amended to recite the phrase "wherein said formulation provides a delayed burst release of venlafaxine *in vivo* after at least two hours following administration." Support for the amendment to claims 89, 91 and 93 can be found in the specification and accompanying figures, particularly, in paragraph 17 of published application No. 20060057204. This amendment is believed to obviate the section 112-second paragraph issue and to better define what Applicant regards as the claimed invention. Upon entry of this communication, claims 88-102 are pending, rejected and are presented for reconsideration.

The Office Action

I. Double Patenting:

Claims 89, 91 and 93 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 42, 43, 45, and 47-49 of copending U.S. Patent application No. 10/555310 in view of U.S. Patent No. 5,840,332. Applicant requests the PTO to hold this provisional double patenting rejection in abeyance until patentable subject matter is identified.

II. Alleged Written Description Rejection

Claims 89-102 are alleged to be in non-compliance with the written description requirement under 35 USC §112-first paragraph. Applicant respectfully traverses.

It is the PTO's contention that the data in the "specification does not provide adequate guidance as to which of the formulations described...." would provide a delayed burst release of venlafaxine *in vitro* after at least two hours. See Office Action at page 5.

Accordingly, the PTO is understood to invite the Applicant to incorporate into the claims a specific combination of ingredients that will provide a formulation that has the recited two hour "lag time" prior to the burst release of venlafaxine as claimed.

As admitted by the PTO (Office Action at page 4), the specification describes in detail the various components of the inventive formulation. Additionally, the specification provides several working examples of the inventive formulations with accompanying data to support the delay in release of venlafaxine for at least two hours as claimed. *See* Figures 1, 2, 4, 6, 8, 10 and 11. The skilled artisan cognizant of the specification, therefore, would readily recognize that Applicant was in possession of a "genus" of formulations capable of providing a burst release venlafaxine after a lag period of at least two hours.

Moreover, as stated in the MPEP § 2163:

> "To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116."

The MPEP further states that "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings...., or by disclosure of relevant, identifying characteristics, i.e., ... by functional characteristics..... sufficient to show the applicant was in possession of the claimed genus..." (MPEP § 2163 II (A) (3) (a)).

Here, the specification, numerous working examples and accompanying figures provide ample guidance that would allow the skilled artisan to formulate a venlafaxine containing "delayed burst release formulation" as claimed.

Thus, the PTO's assertion that the specification lacks descriptive support for the claimed invention is improper and should be withdrawn.

III. Alleged Indefiniteness

Claims 89-102 are rejected under 35 U.S.C. § 112, second paragraph for alleged indefiniteness. *See* Office Action at page 5. Specifically, the PTO states that the phrase "substantially no" is not defined in the specification.

Without acquiescing to the propriety of this rejection, Applicant has amended claims 89, 91, and 93 to delete the objected phrase. This amendment renders the indefiniteness rejection moot.

IV. The Claims Are Patentable Over Sherman in view of Lerner

A. Claims 89-99 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent Number 6,274,171 to Sherman *et al.* (hereafter "Sherman") in view of U.S. Patent Number 5,840,332 to Lerner *et al.* (hereafter "Lerner"). Applicants respectfully traverse.

In support of the rejection, the PTO cites Sherman for its alleged disclosure of a venlafaxine formulation that is capable of providing a delayed burst release as recited in claims 89, 91 and 93. The PTO contends that Sherman discloses a formulation containing a "core of venlafaxine hydrochloride, a filler such as microcrystalline cellulose, which reads on a burst control agent, and water soluble cellulosic polymer such as HPMC..., which reads on the disintegrant..." of the venlafaxine formulation used in the inventive method. According to the PTO, Sherman also discloses coating the core with a water insoluble hydrophobic polymer as claimed. *See* Office Action at page 8.

The PTO admits, however, that Sherman does not teach the presence of hydrophilic particulate matter in the outer coat as claimed. Lerner is cited by the PTO to remedy this deficiency. The PTO concludes by stating that modifying Sherman's formulation to include the hydrophilic particulate matter of Lerner would provide a venlafaxine formulation as claimed, and because the same composition must have the same properties, Sherman's formulation as modified by Lerner's particulate matter should also exhibit the delayed burst release profile as claimed. *Id.*, at 8 and 9. For the reasons below, however, the claims are patentable over Sherman and Lerner.

Contrary to the PTO's characterization of the cited prior art patents, neither Sherman nor Lerner disclose a composition that would allow the delayed **burst release** of venlafaxine after a two hour lag time as claimed.

Sherman teaches an extended release dosage formulation and a unit dosage form of venlafaxine hydrochloride which provides better control of blood plasma levels than conventional tablet formulations. In particular, Sherman teaches an extended release formulation containing spheroids of venlafaxine hydrochloride, microcrystalline cellulose and hydroxypropylmethyl cellulose (HPMC), which spheroids are coated with a mixture of ethylcellulose and HPMC. The coated spheroids of venlafaxine are then filled in a capsule to give a unit dosage form. See col. 3, lines 60-62 and the working examples.

Nowhere, does Sherman teach that the disclosed formulation consisting of coated venlafaxine spheroids in a capsule provide a "burst release" of the drug, much less a delayed burst release as claimed. Support for Applicant's position in this regard is found in Table 1, and the data in the tables accompanying working examples 6 and 7. Table 1 discloses data related to the dissolution rate of capsules according to the formulation disclosed in Sherman. As shown by the data in this table, there is a linear relation between the percent release of venlafaxine hydrochloride as a function of time over a 24 hour period. For example approximately 30% of the drug is release within the first two hours, while the percentage of drug released from the disclosed formulation at 4 hours is around 55% (twice as much drug is released at 4 hours than at 2 hours). The skilled artisan would not understand these results to indicate a formulation that provides **burst release** kinetics as claimed.

Further support that Sherman's formulation does not allow for a burst release of venlafaxine comes from dissolution studies of 16.5 % and 8.25% venlafaxine formulations in working examples 6 and 7 respectively. For both formulations, there is a steady increase in the percentage of venlafaxine released upon dissolution of the capsules as a function of time.

In stark contrast, the formulation used in the inventive method provides a delayed burst release of venlafaxine, that occurs after a two hour lag time following administration. See working examples and accompanying figures. Thus, for formulations disclosed in

working examples 1 and 2, a plot of the percentage of venlafaxine released as a function of time (see figures 1 and 2 respectively), reveals an initial burst of released drug approximately 3 hours after administration, followed by a diffusion controlled release. Such a kinetic profile is not exhibited by Sherman's formulation.

Lerner cited by the PTO does not bridge the gap between the Sherman's formulation and the formulation used in the inventive method. That is, Lerner does not teach a formulation that provides a delayed burst release of venlafaxine, as claimed. The skilled artisan, for example, would have considered it important to note that Lerner teaches the use of particulate water-insoluble material to **control** the "release" of drug, rather than to provide a burst release as recited in the claimed method. See Lerner, abstract and col. 6, lines 17-18 and 23-25. That is, none of the exemplified compositions in Lerner or the accompanying dissolution study data in the figures indicate Lerner's formulation(s) to teach a "burst release" of venlafaxine from the disclosed formulation(s).

Although, the examiner states that Lerner discloses a formulation that provides approximately a 4 hour lag time prior to release of drug (col. 11, line 56 to col. 12, line 2), drug release, however, does not conform to "burst kinetics" as claimed. Thus, modifying Sherman's formulation to include the water insoluble particulate matter disclosed by Lerner would still fail to allow the artisan to arrive at a formulation that has the claimed delayed **burst release**.

The pending obviousness rejection, therefore, is founded on ill-conceived generalization of the Sherman and Lerner disclosures, and withdrawal of the rejection is respectfully requested.

B. Claims 89 -102 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Sherman et al. and Lerner et al. further in view of Upton et al. (US 5,506,270). Applicants respectfully traverse.

The PTO on page 10 comments that Upton is not required to correct the deficiencies of Sherman and Lerner, because the combination of these two references teaches a

formulation as claimed. Thus, the PTO is understood to cite Upton merely for its teaching of a venlafaxine formulation having a dosage of 60 mg.

Contrary to the PTO's commentary on point, as disclosed above, neither Sherman nor Lerner teach a formulation that follows "burst release" kinetics. Thus, even if Upton's teaching of a venlafaxine dosage of 60 mg is incorporated in a formulation of Sherman that has Lerner's water-insoluble particulate matter as suggested by the PTO, the resultant venlafaxine formulation would still be different from the formulation recited in the claims.

Applicant states that the pending claims are patentable over the combined teachings of Sherman, Lerner and Upton and respectfully requests the examiner to withdraw this rejection.

CONCLUSION

Applicant believes that the present application is now in condition for allowance. Should any issues remain that warrant attention, Applicant invites the examiner to contact the undersigned to advance the prosecution.

Respectfully submitted,

Date February 12, 2010

By _____

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 295-4620
Facsimile: (202) 672-5399

Benjamin A. Berkowitz
Attorney for Applicant
Registration No. 59,349

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.